REMARKS

Reconsideration is requested. Claims 1-20 have been canceled, without prejudice. Claims 21-37 have been added and are pending. The claims read on the elected invention and methods of the use of the same. Rejoinder of the pending method claims after allowance of the product claims is requested.

Acknowledgment is requested of the receipt of the certified copy of the priority document by the Patent Office in the parent application Serial No. 09/308,935, during the International Phase of the same (i.e., PCT/GB97/03506), in the Examiner's next Action. See, attached copy of page 1 of Office Action dated May 26, 2000 and copy of Notice of Allowance from Serial No. 09/308,935 wherein Examiner Hunt acknowledged receipt of the certified copy of the priority document. Moreover, acknowledgment of the applicants claim to domestic priority under 35 USC § 120 and/or 121 is requested in the Examiner's next Action.

Figures 1 and 3 have been amended. Figure 1 has been amended to include the sequence identifiers in response to the Examiner's comments spanning pages 2-3 of the Office Action dated June 18, 2003 (Paper No. 11). Figure 3 has been amended to include a designation of the peptides and a reference to the known antiproliferative agent etoposide, consistent with the specification. No new matter has been added.

Acceptance of the formal drawings or specific objection of the same is requested in the Examiner's next Action.

The application is submitted to be in compliance with the Sequence Rules however the Examiner is requested to advise the undersigned if anything further may be required.

Figure 3 has been amended above in response to the Examiner's comments on page 3 of Paper No. 11.

The objection to claims 2-9 stated on pages 3-4 of Paper No. 11 are moot in view of the above. The claims are submitted to be properly dependent.

The Section 112, second paragraph, rejection of claim 9 is moot in view of the above. Claim 29, which is similar to now canceled claim 9, as well as the other pending claims, are submitted to be definite.

The Section 112, first paragraph, rejection of claims 10 and 11 stated on pages 4-9 of Paper No. 11 is moot in view of the above. The claims, such as new claims 30 and 31, are submitted to be supported by an enabling disclosure and consideration of the following in this regard is requested.

The Examiner asserts that "the claims are drawn to a pharmaceutical comprising the peptide claimed in instant claim 1. Inherent in pharmaceutical is *in vivo* use. The specification at page 19 asserts that the peptides claimed could be used in treatment of cancer or psoriasis. The art recognizes that treating cancer and/or psoriasis is not a trivial matter." See, page 5 of Paper No. 11.

Initially, the applicants note that the parent patent (U.S. Patent No. 6,268,334), which contains the same disclosure as the present application, was found to enable claims to a polypeptide of the present invention in a "pharmaceutically acceptable carrier". See, claim 1, for example, of U.S. Patent No. 6,268,334 (copy attached). Claim 1 of the parent patent therefore includes a pharmaceutical which the Patent Office has recognized is supported by an enabling disclosure. The applicants assume the present Examiner is not now asserting a position contrary to a prior Patent Office

determination with regard to patentability however the Examiner is requested to advise the undersigned if otherwise.

The applicants note further that the present application provides experimental details in which, for example, Example E demonstrates that polypeptides of the invention activate a cell's apoptopic programme (page 28). Moreover, Example F of the present application demonstrates that the combination of the known antiproliferative agent etoposide with a polypeptide of the present invention caused high level of cell death indicating an additive affect. These results are an indication that the compounds in the invention are useful in reducing unwanted cell proliferation by the induction of, for example, apoptosis and hence that the polypeptides of the invention can be used in the treatment of conditions involving unwanted cell proliferation, such as cancer. Moreover, while not believed to be required to support patentability, the mechanism of the involvement of the peptides of the invention in apoptosis is described, for example, at page 18, lines 7-14 of the present application. One of ordinary skill in the art would be able to make and use the presently claimed invention, such as is defined in claims 30 and 31, without undue experimentation.

As for the Examiner's cited art, the applicants respectfully submit that, as an initial matter, none of the cited art has reviewed the present application and opined as to whether the present application teaches one of ordinary skill in the art how to make and use the presently claimed invention, as required by Section 112, first paragraph. Accordingly, the cited art is believed to be of limited relevance.

More specifically, the applicants note that the cited Gura reference (Science, 1997, 278:1041-1042), describes difficulties in using animal models of cancer to predict

drugs which will "win" approval from the U.S. Food and Drug Administration. See, page 1041, left column, second paragraph of Gura. The Examiner will appreciate that patentability is not based on "winning" U.S. Food and Drug Administration approval. That is, the standards are quite different between enablement required under Section 112, first paragraph, for obtaining a patent to a pharmaceutical composition and evidence required to bring a drug to market. Accordingly, the motivation of Gura in criticizing currently available models for testing cancer therapeutics is unrelated to the requirements for enablement under Section 112, first paragraph, of the patent statute.

Moreover, the applicants believe that Gura criticizes the use of xenographs as a model for testing "effective drugs". See, page 1041 left column, third paragraph of Gura and generally page 1041. The patent statute and Court decisions relating to patentability require disclosure sufficient to make and use a claimed chemical invention, for example, without undue experimentation as opposed to disclosure of only the best or most or only "effective" drugs.

The Examiner will appreciate that the results of Examples E and F of the present application do not involve the use of xenographs. In fact, Examples E and F of the present application include cell culture techniques wherein a cell line (i.e., 3T3 cells) has been used in testing as a predictive model. Gura teaches that the National Cancer Institute (NCI) has now adopted testing of drug candidates in cultures of human cells, as opposed to the earlier used and now criticized use of xenographs. See, page 1042, left column, of Gura. Accordingly, one of ordinary skill in the art, such as researchers at NCI, would apparently approve of the use of cell culture techniques for testing, as demonstrated in the present application.

Moreover, Alan Oliff, executive director for cancer research at Merck Research Laboratories in West Point, Pennsylvania, is quoted in the concluding paragraph of Gura as stating that "the future of cancer drug screening is turning almost exclusively toward defining molecular targets." The applicants note the mechanism of cancer treatment described in the present application at page 18, lines 7-14, while not being required to support patentability, is apparently consistent with Mr. Oliff's expectations for the then future of cancer research. Such examples of the present specification therefore are apparently well recognized and appreciated by those of ordinary skill in the art at the time of the present invention.

Accordingly, rather than indicating that one of ordinary skill in the art would not have been able to make and use the presently claimed invention, Gura is seen, if anything, to support the applicants belief that one of ordinary skill in the art would have been able to make and use the claimed invention from the teachings of the specification and generally advanced level of skill in the art.

The Examiner's reliance on Fan et al. (2003, PNAS, Vol. 100, pages 3386-3391), appears to be an attempt to suggest that psoriasis is merely an immunological disease which would not be expected to be treated by a peptide of the presently claimed invention. The applicants note however that, at least according to the attached two-page printout from a Boston University website ("www.bu.edu/cme/modules/2002/psoriasis02/content/1-gen.htm"), psoriasis is a hyperproliferative disorder of the skin which specifically involves keratinocytes in the epidermis. This hyperproliferation of keratinocytes involves a greatly increased turnover

of the epidermis from 27 days to 4-6 days. See, attached 2-page printout from the Boston University website.

As noted above, the Patent Office has granted the applicants claims in the parent U.S. Patent No. 6,268,334 (face page and claims of which are attached) wherein claims were granted to a surgical stent comprising a coating incorporating a polypeptide in a pharmaceutically acceptable carrier, wherein the polypeptide may be a polypeptide of the present invention which antagonizes the formation of a DP/E2F. Page 20, lines 12-25 of the present application, for example, describes that such a stent may be useful, for example, in preventing local regrowth of cell by antagonizing entry of the cells though the cell cycle. One or ordinary skill in the art would believe, from the present specification as well as the advanced level of skill in the art, that such a prevention of local regrowth may be useful in a disease involving hyperproliferation of cells such as psoriasis. The Examiner has not indicated where Fan suggests anything to the contrary. The presently claimed invention is believed to be supported by an enabling disclosure.

The Examiner's reliance on Jain (Scientific American, July 1994, pages 58-65) is further believed, with due respect, to be irrelevant to the question as to whether the presently claimed invention is supported by an enabling disclosure. The Examiner appears to rely on Jain to allegedly establish a recognition that "scientist need to put expanded effort into uncovering the reasons why therapeutic agents that show encouraging promise in the laboratory often turn out to be ineffective in the treatment of common solid tumors." See, the sentence spanning pages 5-6 of Paper No. 11. Whether scientists should put expanded efforts into uncovering the reasons why

therapeutic agents that show encouraging promise in a laboratory often turn out to be ineffective in the treatment of common solid tumors is not however a question which is relevant to the issue of whether the presently claimed invention is supported by an enabling disclosure. Jain, like the Curti reference discussed below, are reports of generally academic pursuits which, while important in refining drug delivery, for example, are not believed to be germane to the issue of enablement of the claimed invention.

As the present application provides assay methods to test drug candidates such as are described on page 5, line 27 to page 6, line 3 and page 18, line 18 to page 19, line 10, the present disclosure may facilitate scientists efforts into uncovering the reasons why therapeutic agents that show promise in laboratories often turn out to be ineffective in the treatment of common solid tumors. Such a quest for elucidation of basic research mechanisms however is not required for enablement under the patent statue. Interestingly enough, much of Jain's description of methodology appears to include the use of xenographs which are criticized by the Gura reference cited by the Examiner.

The Examiner's comments with regard to Curti (Critical reviews in Oncology/Hematology, 1993; 14:29-39), relate to mechanisms to deliver chemotherapeutic agents to solid tumors. Curti appears to be similar to Jain in its consideration of academic and theoretical modeling of different transport mechanisms relating to drug delivery. As noted above, a pharmaceutically useful embodiment of the presently disclosed invention has been acknowledged by the Patent Office to be supported by an enabling disclosure. The knowledge or explanation of the mechanism

of an invention is not required under the patent statute. More importantly, development of better or the best or the most efficient delivery mechanism and its theoretical and academic modeling, such as are investigated by Curti and Jain, are not required to enable one of ordinary skill in the art to make and use a pharmaceutical composition which, in certain embodiments, may be used for the treatment of cancer. The applicants submit, with all due respect, that the Examiner's reliance on Curti in an attempt to establish that one of ordinary skill in the art could not have made and used the presently claimed invention is misplaced. Moreover, the Examiner's assertion that "it is clear that based on the state of the art, in the absence of experimental evidence, no one skilled in the art would accept the assertion that the claim peptide would be useful for treating cancer" is unsupported and unjustified.

The Examiner's reliance on Hartwell (Science, Vol. 278, 7 November 1997, pages 1064-1068), as teaching that "anticancer drugs have been discovered by serendipity and that the molecular alternations that provide selective tumor cell killing are unknown and that even understanding the detailed molecular mechanisms by which a drug acts often provides little insight into why the treated tumor cell dies" (see, page 6 of Paper No. 11), is believed to be contrary to the statements of Alan Oliff quoted above from the Gura reference relied upon by the Examiner. Specifically, as noted above, Mr. Oliff states that the future of cancer drug screening is turning almost exclusively toward defining molecular targets. The Examiner also relies on the apparent contrary statement of Hartwell that understanding the details of molecular mechanisms by which drugs act will provide little insight into developing cancer therapies. It is unclear what the Examiner believes one of ordinary skill would find convincing or persuasive.

To the extent the Examiner is relying on Hartwell, or any of the references, to assert that the presently claimed invention could not reasonably be used to, for example, selectively kill cancer cells, the applicants respectfully submit that such selective killing is not required at least for patentablity purposes and that many chemotherapeutic agents being currently used in patients do not selectively kill cancer cells or at least do not do it very well. Certainly, it is a goal of chemotherapeutic research to develop such selective chemotherapeutic agents.

To this end, the applicants note that Hartwell describes a distinction of tumor cells which may be exploited in developing such chemotherapeutic agents. Specifically, Hartwell describes that tumor cells universally exhibit genetic instability. According to Hartwell, the "best single documentation of this... is that many tumor cells from different origins have been examined for their ability to undergo gene amplification and all exhibit high rates of gene amplification in comparison with normal untransformed cells." See, page 1065, middle column of Hartwell. This appears to suggest that one of ordinary skill in the art would appreciate that a therapy directed at high rates of gene amplification, such as aberrant proliferating cells, would have a reasonable expectation of being successful. See, attached explanation of psoriasis. As noted on page 2 of the present application, for example, a mechanism of the presently claimed invention may target and exploit this difference between tumor cells and normal cells. Accordingly, Hartwell, demonstrates, if anything, that one of ordinary skill in the art would have a reasonable expectation that the presently claimed invention could be made and used without undue experimentation.

The Examiner's comments at page 7 of Paper No. 11 appear to be directed to requirements for FDA approval of a new drug as opposed to enablement of a patentable invention and are submitted to be more than required by the patent statute.

The Examiner's reliance on Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, page 4) and related comments on pages 7-8 of Paper No. 11 appear to be contrary to the statements in Gura indicating that the National Cancer Institute is now using cell culture techniques to test new chemotherapeutic agents. The Examiner's apparent requirements for *in vivo* testing are more than is required by the patent case law. The fact that Freshney may teach that there are many differences between cultured cells and their counterparts *in vivo*, which appears to be the basis for the Examiner's reliance on the same, the National Cancer Institute appears to believe otherwise as to the predictive capacity of in vitro testing. Similar comments apply to the Examiner's reliance on Dermer (Bio/Technology, 1994, 12:320) which was published prior to Gura.

The claimed invention is submitted to be supported by an enabling disclosure.

The Section 102 rejection of claims 1-9 over U.S. Patent No. 5,863,757 (La Thangue) is moot in view of the above. The claimed invention is submitted to be patentable over the cited art and consideration of the following in this regard is requested.

The Examiner is understood to allege that the now-canceled claims are to be interpreted to include any DP-1 polypeptide shorter than the full length (410 amino acid) DP-1 polypeptide. According to the Examiner, this interpretation is based on page 6, lines 19-27 of the present application.

The indicated SEQ ID NO:11 of U.S. Patent No. 5,863,757 is a 72 amino acid sequence which contains within it the 37 amino acid sequence of SEQ ID NO:1 of the presently claimed invention.

The section of the description referred to by the Examiner states that the application provides a "polypeptide consisting essentially of SEQ ID NO:1" and that "by 'consisting essentially' it is meant that the sequence is not, .. part of a larger peptide sequence", although the presence of from 1 to 5 amino acids at either or both of the N and C terminus is not excluded [emphasis added]. The applicants believe that one of ordinary skill would interpret the claim recitation of "consisting essentially of" to indicate that the polypeptide of now canceled claim 2, for example, of the present application can, at the most, be 37 amino acids plus from 1 to 10 amino acids, i.e. 1-5 from either terminus and a maximum of 47 amino acids in length. This is considerably shorter than the full length DP-1 polypeptide having 410 amino acids and also significantly shorter than the 72 amino acid polypeptide which is SEQ ID NO:11 of U.S. Patent No. 5,863,757.

The claims are patentable over U.S. Patent No. 5,868,757.

The Section 102 rejection of claims 2-9 over U.S. Patent No. 5,859,199 (La Thangue) is moot in view of above. The claims are submitted to be patentable over La Thangue and consideration of the following in this regard is requested.

As noted above, the Examiner's interpretation of the claims is not correct in light of the teaching of the specification. In the event the rejection is maintained, the Examiner is requested to identify specifically those peptides of the cited patent which are believed to anticipate the presently claimed invention. The search results attached

to the Office Action may become separated from the Patent Office records and a complete record is requested in this regard. Moreover, the search results are cryptic in their description, if any, of the basis for the rejection. As none of the peptides disclosed in the cited patent teach or suggest the presently claimed invention, as described above and in the specification, the reference fails to teach each and every aspect of the presently claimed invention. The claims are submitted to be patentable over U.S. Patent No. 5,859,199.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned if anything further is required in this regard.

Respectfully submitted,

NIXON & VANDERHYE P.C.

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Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

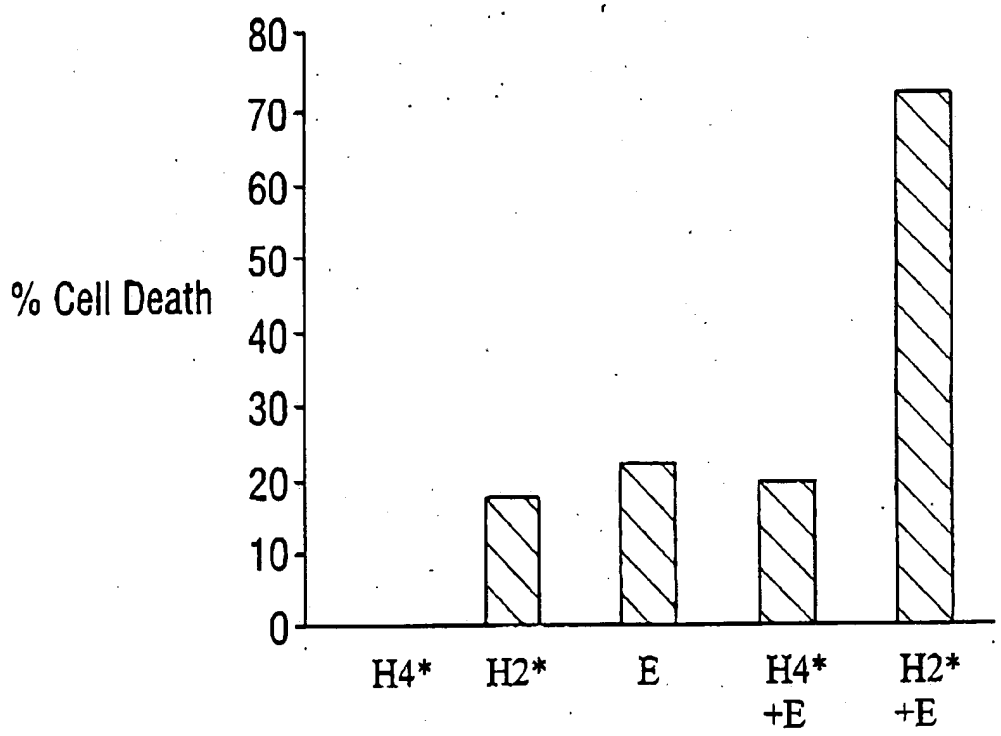
FIG. 1

		163 :	199 :	Activity Dimer	DB
SEQ ID NO:1	H	KNIRRRVYDALNVLMAMNIISKEKKEIKWIGLPTNSA		+	+
SEQ ID NO:9	H1	RRRVYDALNVL		-	-
SEQ ID NO:3	H2	RRRVYDALNVLMAMNIISK		+	+
SEQ ID NO:4	H3	NVLMAMNIISKEKKEIKWIG		+	+/-
SEQ ID NO:10	H4	EKKEIKWIGLPTNSA		-	-
SEQ ID NO:5	H5	RVYDALNVLMAMNIIS		+	+/-
SEQ ID NO:11	H6	RRVYDALNVLMAMN		-	-
SEQ ID NO:6	H7	YDALNVLMAMNIISKEKKEIKWIGLPTNSA		+	+
SEQ ID NO:12	18	NESAYDQKNIRR		-	-
SEQ ID NO:13	15	NLVQRNRQAEQQARR		-	-
SEQ ID NO:14	17	EVERQRRLERIKQKQ		-	-

1/3

Inventor: LA THANGUE et al
SN 09/900,147/Sheet 3 of 3
Atty. Dkt.: 620-149

FIG. 3



E = etoposide

US006268334B1

(12) **United States Patent**
La Thangue et al.

(10) **Patent No.: US 6,268,334 B1**
(45) **Date of Patent: Jul. 31, 2001**

(54) **PEPTIDE ANTAGONISTS OF DP TRANSCRIPTION FACTORS**

(75) Inventors: **Nicholas B. La Thangue**, Glasgow; **Lasantha R. Bandara**, Abingdon, both of (GB)

(73) Assignee: **Prolifix Limited**, Abingdon (GB)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/308,935**

(22) PCT Filed: **Dec. 22, 1997**

(86) PCT No.: **PCT/GB97/03506**

§ 371 Date: **May 27, 1999**

§ 102(e) Date: **May 27, 1999**

(87) PCT Pub. No.: **WO98/28334**

PCT Pub. Date: **Jul. 2, 1998**

(30) **Foreign Application Priority Data**

Dec. 20, 1996 (GB) 9626589

(51) **Int. Cl.**[7] **A01N 37/18**; A61K 38/00; C01K 14/00; C01K 16/00; C01K 17/00

(52) **U.S. Cl.** **514/2**; 530/300

(58) **Field of Search** 536/23.1; 514/2; 530/300

(56) **References Cited**

PUBLICATIONS

L.R. Bandara et al.: "Apoptosis induced in mammalian cells by small peptides that functionally antagonise the Rb–regulated E2F transcription factor" Nature Biotechnology, vol. 15, Sep. 1997, pp. 896–901, XP002061239 see the whole document.

L.R. Bandara et al.: "Functional synergy between DP–1 and E2F–1 in the cell cycle–regulating transcription factor DRTF1/E2F" Embo Journal., vol. 12, No. 11, 1993, Eynsham, Oxford GB, pp. 4317–4324, XP002061240 cited in the application see the whole document. See page 4320, column 1, paragraph 3; see p. 4232, column 2, paragraph 3; see p. 4320, column 2, paragraph 2; see figure 2E.

Wu C–L et al: "In Vivo Association of E2F and DP Family Proteins" Molecular and Cellular Biology, vol. 15, No. 5, May 1995, pp. 2536–2546, XP002041648 see figure 1.

D. Derossi et al.: "The third helix of the antennapedia homeodomain translocates through biological membranes" Journal of Biological Chemistry., vol. 269, No. 14, 1994, MD US, pp. 10444–10450, XP002061241 cited in the application see the whole document.

Wu et al., In Vivo Association of E2F and DP Family Proteins, Molecular and Cellular Biology, vol. 15, No. 2, p. 2536–2546, May 1995.*

Girling et al., A new component of the transcription factor DRTF1/E2F, Nature, Vol. 362, p. 83–87, Mar. 1993.*

Dermer, Another Anniversary for the War on Cancer, Bio/Technology, vol. 12, p. 320, May 1995.*

* cited by examiner

Primary Examiner—Anthony C. Caputa
Assistant Examiner—Jennifer Hunt
(74) *Attorney, Agent, or Firm*—Nixon & Vanderhye P.C.

(57) **ABSTRACT**

The invention provides a polypeptide consisting essentially of a sequence corresponding to residues 163 to 199 of DP-1 as shown in the Figure, and fragments and variants thereof capable of antagonising the heterodimerization of a DP protein with an E2F protein. Such peptides may be used to induce apoptosis in a cell by introducing into the cell an effective amount of said peptide. Such cells include cardiovascular cells, and the peptide may be delivered in a stent to treat or prevent restinosis.

10 Claims, 3 Drawing Sheets

	163 :	199 :	Activity Dimer	DB
H	KNIRRRVYDALNVLMAMNIISKEKKEIKWIGLPTNSA		+	+
H1	RRRVYDALNVL		-	-
H2	RRRVYDALNVLMAMNIISK		+	+
H3	NVLMAMNIISKEKKEIKWIG		+	+/-
H4	EKKEIKWIGLPTNSA		-	-
H5	RVYDALNVLMAMNIIS		+	+/-
H6	RRVYDALNVLMAMN		-	-
H7	YDALNVLMAMNIISKEKKEIKWIGLPTNSA		+	+
18	NESAYDQKNIRR		-	-
15	NLVQRNRQAEQQARR		-	-
17	EVERQRRLERIKQKQ		-	-

pg 20, lines 12-25
[illegible] cells
by [illegible] cells
[illegible] through the cell [illegible]

-continued

<210> SEQ ID NO 16
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Mutant peptide

<400> SEQUENCE: 16

Arg Ala Arg Val Tyr Ala Ala Leu Asn Val Leu Met Ala Met Asn Ile
1 5 10 15

Ile Ser Lys

<210> SEQ ID NO 17
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Mutant peptide

<400> SEQUENCE: 17

Arg Arg Arg Val Tyr Asp Ala Arg Asn Val Arg Met Ala Met Asn Ile
1 5 10 15

Ile Ser Lys

<210> SEQ ID NO 18
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Oligonucleotide

<400> SEQUENCE: 18

cgtgtctacg atggcggaaa tgtgctaatg 30

What is claimed is:

1. A surgical stent which comprises a coating incorporating a polypeptide in a pharmaceutically acceptable carrier, the polypeptide consisting of the amino acid sequence of SEQ ID NO: 3, or a variant thereof having from 1 to 5 amino acid substitutions, the variant retaining the ability to antagonize the formation of a DP/E2F.

2. The stent of claim 1 wherein said variant includes a substitution selected from one or more residues corresponding to residues 167, 169, 171 and 175 of DP-1.

3. The stent of claim 1 wherein said variant consists of the amino acid sequence of SEQ ID NO: 15.

4. The stent of claim 1 wherein said variant consists of the amino acid sequence of SEQ ID NO: 16.

5. A surgical stent which comprises a coating incorporating a polypeptide in a pharmaceutically acceptable carrier, the polypeptide consisting of the amino acid sequence of SEQ ID NO: 3, or a variant thereof having from 1 to 5 amino acid substitutions, the variant retaining the ability to antagonize the formation of a DP/E2F heterodimer, wherein said polypeptide is fused at its N- or C-terminus to a membrane translocation sequence.

6. The stent of claim 5 wherein said membrane translocation sequence is derived from the *Drosophila melanogaster* antennapedia protein.

7. A surgical stent which comprises a coating incorporating a polypeptide in a pharmaceutically acceptable carrier, the polypeptide consisting of the amino acid sequence of SEQ ID NO: 3 and, from 0 to 5 amino acids at the N- or C-terminus, or a variant thereof having from 1 to 5 amino acid substitutions, the variant retaining the ability to antagonize the formation of a DP/E2F heterodimer.

8. The stent of claim 7, wherein said variant includes a substitution selected from one or more residues corresponding to residues 167, 169, 171 and 175 of DP-1.

9. The stent of claim 7, wherein said variant consists of the amino acid sequence of SEQ ID NO: 15.

10. The stent of claim 7, wherein said variant consists of the amino acid sequence of SEQ ID NO: 16.

* * * * *

Psoriasis

Psoriasis: General Information

Epidemiology

Psoriasis occurs in 1-4% of the population worldwide. It is a common, chronic hyperproliferative disorder of the skin. Of the 150,000 to 260,000 new cases per year, men and women are affected equally. Typically, onset is during the 3rd decade of life, although age of onset may be from birth to the eighth decade of life. There is an increased severity o this disease with HIV infection.

Etiology

The etiology of psoriasis is hyperproliferation of the keratinocytes in the epidermis. The normal turnover time of the epidermis is 27 days: in a psoriatic plaque, the turnover time is reduced to 4-6 days. There is a two-fold increase in the proliferative cell population. The role of the immune system is important in the development of psoriasis: there is a strong association of the disease with HLA-Cw6, HLA-B13, and HLA-B57. In addition, a great number of CD4 positive lymphocytes (helper T-cells) are present within psoriatic lesions. Finally, multiple cytokines have been demonstrated to play a role in psoriasis, including IL 1, IL-6, IL-8, TGF-alpha, and PDGF.

Genetics

The association of psoriasis with specific major histocompatibility antigens has been discussed. A genetic transmission of psoriasis has been indicated by numerous studies: the mode of transmission may be autosomal dominant with variable penetrance or may be polygenic. A familial susceptibility gene has been demonstrated on the distal end of chromosome 17q.

General Clinical Manifestations

Psoriasis is a life-long disease with exacerbations and remissions. It can be emotionally troubling. The distinctive cutaneous findings include well-demarcated erythematous plaques, thickening of the skin, and a silvery, loosely adherent scale. Psoriasis has a tendency to develop in sites of trauma: this is known as Koebner's phenomenon. Pruritus is variable. Certain areas of the skin have a greater tendency for involvement: these include the elbows, knees, scalp, lower back, intergluteal cleft, and genitalia. Fingernails and toenails may be involved, with pitting, yellow "oil spots", and onycholysis.

Certain triggering factors for psoriatic flares have been identified: these include physical trauma, medications (Lithium and beta-blockers especially), infections (including HIV), alcohol ingestion, and stress.

Systemic associations have been identified with psoriasis. These include arthritis (present in 5-8% of all psoriasis patients, and in greater than 10% of those with severe psoriasis), increased serum uric acid levels (presumably due to increased cell turnover), and mild anemia.

Top | Course outline | Previous page | Next page

620-67
BJS

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Patent and Trademark Office
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Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/308,935	05/27/99	LI THANGUE	N 620-67

EXAMINER
HUNT, J

ART UNIT.	PAPER NUMBER
1642	7

DATE MAILED: 05/26/00

HM12/0526

NIXON & VANDERHYE
1100 NORTH GLEBE ROAD
8TH FLOOR
ARLINGTON VA 22201-4714

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

DOCKETED
CLT/MATTER # 620-67
MAIL DATE 5/26/00
DUE DATE August 26, 2000
FINAL DEADLINE Nov. 26, 2000
DOCKETED BY MK/MR

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PTO-90C (Rev. 2/95)

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Office Action Summary

Application No.	Applicant(s)
09/308,935	LA THUNGE et al.
Examiner	**Group Art Unit**
Jennifer Nichols, Nee Hunt	1642

☐ Responsive to communication(s) filed n _____

☐ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-20 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-20 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Offic

VB

NOTICE OF ALLOWANCE AND ISSUE FEE DUE

HUNT, 0227

NIXON & VANDERHYE
1100 NORTH GLEBE ROAD
8TH FLOOR
ARLINGTON VA 22201-4714

APPLICATION NO.	FILING DATE	TOTAL CLAIMS	EXAMINER AND GROUP ART UNIT	DATE MAILED
09/308,935	05/27/99	010	HUNT, J	02/27/01

First Named Applicant: LA THANGUE,

35 USC 154(b) term adj. 0 Days.

TITLE OF INVENTION: PEPTIDE ANTAGONISTS OF UP TRANSCRIPTION FACTORS

ATTY'S DOCKET NO.	CLASS-SUBCLASS	BATCH NO.	APPLN. TYPE	SMALL ENTITY	FEE DUE	DATE DUE
1 620-67	514-002.000	071	UTILITY	NO	$1240.00	05/29/01

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED.

THE ISSUE FEE MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED.

HOW TO RESPOND TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.
If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is changed, pay twice the amount of the FEE DUE shown above and notify the Patent and Trademark Office of the change in status, or
B. If the status is the same, pay the FEE DUE shown above.

If the SMALL ENTITY is shown as NO:

A. Pay FEE DUE shown above, or

B. File verified statement of Small Entity Status before, or with, payment of 1/2 the FEE DUE shown above.

II. Part B-Issue Fee Transmittal should be completed and returned to the Patent and Trademark Office (PTO) with your ISSUE FEE. Even if the ISSUE FEE has already been paid by charge to deposit account, Part B Issue Fee Transmittal should be completed and returned. If you are charging the ISSUE FEE to your deposit account, section "4b" of Part B-Issue Fee Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give application number and batch number.
Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

YOUR COPY

Notice of Allowability

Application No.	Applicant(s)
09/308,935	LA THUNGE et al.
Examiner	**Group Art Unit**
Jennifer Hunt	1642

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance and Issue Fee Due or other appropriate communication will be mailed in due course.

☒ This communication is responsive to *the amendment after final filed 2-05-2001*.

☒ The allowed claim(s) is/are *17 and 21-29*.

☐ The drawings filed on _____ are acceptable.

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

A SHORTENED STATUTORY PERIOD FOR RESPONSE to comply with the requirements noted below is set to EXPIRE THREE MONTHS FROM THE "DATE MAILED" of this Office action. Failure to timely comply will result in ABANDONMENT of this application. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

☐ Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION, PTO-152, which discloses that the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.

☒ Applicant MUST submit NEW FORMAL DRAWINGS

☐ because the originally filed drawings were declared by applicant to be informal.

☒ including changes required by the Notice of Draftsperson's Patent Drawing Review, PTO-948, attached hereto or to Paper No. _____.

☐ including changes required by the proposed drawing correction filed on _____, which has been approved by the examiner.

☐ including changes required by the attached Examiner's Amendment/Comment.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the reverse side of the drawings. The drawings should be filed as a separate paper with a transmittal lettter addressed to the Official Draftsperson.

☐ Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Any response to this letter should include, in the upper right hand corner, the APPLICATION NUMBER (SERIES CODE/SERIAL NUMBER). If applicant has received a Notice of Allowance and Issue Fee Due, the ISSUE BATCH NUMBER and DATE of the NOTICE OF ALLOWANCE should also be included.

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

☒ Interview Summary, PTO-413

☒ Examiner's Amendment/Comment

☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material

☐ Examiner's Statement of Reasons for Allowance